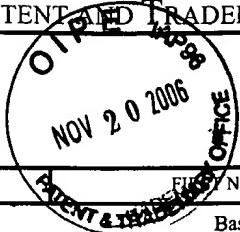




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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO.   | CONFIRMATION NO. |
|-----------------|-------------|----------------------|-----------------------|------------------|
| 09/782,004      | 02/12/2001  | Bassil I. Dahiyat    | A-67229-6/RFT/RMS/RMK | 1900             |
| 7590            | 11/09/2006  |                      | EXAMINER              |                  |
|                 |             |                      | BORIN, MICHAEL L      |                  |
|                 |             |                      | ART UNIT              | PAPER NUMBER     |
|                 |             |                      | 1631                  |                  |

DATE MAILED: 11/09/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

NOV 20 2006

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**Application No.**

09/782,004

**Applicant(s)**

DAHIYAT ET AL.

**Examiner**

Michael Borin

**Art Unit**

1631

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
  - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
  - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) Responsive to communication(s) filed on 29 June 2006.
- 2a) This action is FINAL.                    2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) Claim(s) 12,13,21-24 and 33-35 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 12,13,21-24,33-35 is/are rejected.
- 7) Claim(s) \_\_\_\_\_ is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All    b) Some \* c) None of:
  1. Certified copies of the priority documents have been received.
  2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) Notice of References Cited (PTO-892)
- 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date 06/29/2006.

- 4) Interview Summary (PTO-413)

Paper No(s)/Mail Date. \_\_\_\_\_.

- 5) Notice of Informal Patent Application

- 6) Other: \_\_\_\_\_.

## **DETAILED ACTION**

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 06/29/2006 has been entered.

### ***Status of Claims***

1. Claims 12,13,21-24,33-35 are pending.

### ***Claim Rejections - 35 USC § 112, second paragraph.***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 12,13,21-24,33-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 12, step c): It remains not clear how residues are being "selected" from a plurality of positions of plurality of sequences.

***Claim Rejections - 35 USC § 112, first paragraph.***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 12,13,21-24,33-35 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Claims 12,33-35 introduce new matter as they use the "selecting amino acid residues from ... said ranked primary variant proteins". The above indicated subject matter is not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

***Claim Rejections - 35 U.S.C. § 101/ 112-1***

4. Claims 12,13,21-24,33-35 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific asserted utility or a well established utility.

The rejection is maintained for the reason of record.

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Applicant submits that the “real world” utility of the method is in reducing amount of variant sequences<sup>1</sup>. Examiner maintains that the method remain to be directed to generation of yet another library, secondary library of protein variants, which variants are a combination of amino acid residues selected from variant protein sequences of the first library. Thus, the instantly claimed method provides for generating a secondary library of as yet undetermined structure, function or biological significance which is obtained by a random combination of amino acid residues derived from a plurality of variant positions. As specification teaches ( paragraph [0103]) that

... in general, the variant positions and/or amino acid residues in the variant positions can be recombined in any number of ways to form a new library that exploits the sequence variations found in the primary library,

one can envision that the secondary library will be comprised of a random permutation of all natural amino acid residues. Utility of such random library is not addressed neither in specification, nor in applicant’s response.

Until some actual and specific significance can be attributed to the secondary library or even the compounds present the library, an artisan would be required to perform additional experimentation in order to determine how to use the generated secondary library. Thus, there was no immediate “real world “ utility as of the filing date. Because any potential pharmacological or any other utility is not yet known and has not yet been disclosed, the utility is not substantial because it is not currently available in any specific and practical form.

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<sup>1</sup> It is noted that applicant applies argument related to “useful, concrete, and tangible” criteria. This argument is relevant to 101, non-statutory, rejection, rather than to utility rejection.

Therefore, the claimed method secondary library of as yet undefined structure generated from the claimed method does not have a specific and substantial or real-world utility well-established utility.

5. Claim 12,13,21-24,33-35 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either as asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

#### **Claim Rejections - 35 U.S.C. § 101 (non-statutory invention)**

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

6. Claims 12,13 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claims 12,13 are drawn to computational method of generating secondary library of protein variants.

The following analysis of facts of this particular patent application follows the analysis suggested in the "Interim Guidelines for Examination of Patent Applications for

Patent Subject Matter Eligibility<sup>2</sup>. Note that the text of the Guidelines below is italicized.

*To satisfy section 101 requirements, the claim must be for a practical application of the § 101 judicial exception, which can be identified in various ways*

- *The claimed invention “transforms” an article or physical object to a different state or thing.*
- *The claimed invention otherwise produces a useful, concrete and tangible result, based on the factors discussed below.*

In the instant case, the claimed invention does not “transform” an article or physical object to a different state or thing. This does not preclude the subject matter to be patentable as, for eligibility analysis, as

*physical transformation is not an invariable requirement, but merely one example of how a mathematical algorithm [or law of nature] may bring about a useful application. If the examiner determines that the claim does not entail the transformation of an article, then the examiner shall review the claim to determine if the claim provides a practical application that produces a useful, tangible and concrete result. In determining whether the claim is for a “practical application,” the focus is not on whether the steps taken to achieve a particular result are useful, tangible and concrete, but rather that the final result achieved by the claimed invention is “useful, tangible and concrete.” The claim must be examined to see if it includes anything more than a § 101 judicial exception. If the claim is directed to a practical application of the § 101 judicial exception producing a result tied to the physical world that does not preempt the judicial exception, then the claim meets the statutory requirement of 35 U.S.C. § 101. If the examiner does not find such a practical application, the examiner has determined that the claim is nonstatutory. (Guidelines, p. 20)*

The question is thus whether the final result achieved by the claimed invention is a result which satisfies all three criteria of being useful, and concrete, and tangible. In determining if the instant claims are useful, tangible, and concrete, the Examiner must determine each standard individually. For a claim to be “useful,” the claim must produce a result that is specific, substantial, and credible. For a claim to be “tangible,” the claim must set forth a practical application of the invention that produces a real-world result. For a claim to be “concrete,” the process must have a result that can be

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<sup>2</sup> Available at [http://www.uspto.gov/web/offices/pac/dapp/ropa/preognotice/guidelines101\\_20051026.pdf](http://www.uspto.gov/web/offices/pac/dapp/ropa/preognotice/guidelines101_20051026.pdf)

substantially repeatable or the process must substantially produce the same result again.

Furthermore, the useful, tangible, and concrete result must be either explicitly recited in the claim itself or inherently flown through therefrom; rather than merely addressed in the specification.

In addition, a claim must be limited only to statutory embodiments - thus, if the claim is broader than the statutory embodiments of the claim, the Examiner must reject the claim as non-statutory.

#### **(1) "USEFUL RESULT"**

*When the examiner has reason to believe that the claim is not for a practical application that produces a useful result, the claim should be rejected, thus requiring the applicant to distinguish the claim from the three § 101 judicial exceptions to patentable subject matter by specifically reciting in the claim the practical application. In such cases, statements in the specification describing a practical application may not be sufficient to satisfy the requirements for section 101 with respect to the claimed invention.* Guidelines, p. 21.

If the claimed invention does not produce a useful result, i.e. fulfill any of the disclosed utilities, determine if any utility of the claimed result would have been recognized by those in the art as being specific, substantial and credible. If no utility for the result would have been recognized, then the claim must be rejected as non-statutory for failing to comply with 35 USC 101, i.e., not providing a useful, concrete and tangible result. (Training Materials)

For an invention to be "useful" it must satisfy the utility requirement of section 101, i.e., it has to be (i) specific, (ii) substantial and (iii) credible. As discussed in the utility rejection above, the invention does not satisfy the criteria of utility requirements as not being specific and substantial. Further, if the specification discloses a practical application of a § 101 judicial exception, but the claim is broader than the disclosure such that it does not require a practical application, then the claim must be rejected. In the instant case, the claims encompass a computational method of generating a library

of protein variants comprising a random assortment of residues selected from plurality of primary variant protein sequences.

**(2) "TANGIBLE RESULT"**

*The tangible requirement does not necessarily mean that a claim must either be tied to a different state or thing. However, the tangible requirement does require that the claim must recite more than a § 101 judicial exception, in that the process claim must set forth a practical application of that § 101 judicial exception to produce a real-world result. The opposite meaning of "tangible" is "abstract."*

In the instant case the instant claims are drawn to computational means for generating a library of protein variants. However, as claimed, the method does not include a real world result as the method as claimed may take entirely within the confines of a computer without any communication to the outside world. A tangible requirement requires that the claim must set forth a practical application of the computational steps to produce a real-world result. As the claim does not recite communication of a result in a tangible form to one performing the method the instant claims do not include any tangible result.

Therefore, the claims are rejected as non-statutory for failing to comply with 35 USC 101, i.e., not providing a useful, concrete and tangible result.

***Claim Rejections - 35 USC § 102 and 103***

The following are previously applied rejections of record which have been temporarily withdrawn in view of claim amendments containing new matter.

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7. Claims 12,13,33-35 are rejected under 35 U.S.C. 102(e) as being anticipated by Lacroix et al (US 2002/0072864; filing date 08/31/1999).

US 2002/0072864 teaches computer-based method for macromolecular engineering wherein the method comprises steps of

- a) inputting coordinates of said protein into a computer (see, e.g., claims 12,13);
- b) using various force field calculations (see sections 5.4.1; 5.8.1; 5.9.2)
- c) combining, after subsequent steps, candidates for the target structures (see section 5.11).

With respect to limitation of claims 12,35, that at least one of secondary variant proteins is different from primary variant proteins, Lacroix's method considers "the immense variety of sequences that can be generated as a result of protein mutagenesis, i.e., substitution of one amino acid side chain with a different amino acid side chain at a given site in the protein". Thus, the resulting set can be different from original variant. The claims, however, are addressed to their maximum breadth, and both "primary" and "secondary" library are viewed simply as collections of amino acid residues. In addition, the results of the computational steps of Lacroix is a subset of optimized structures, which conforms to the definition of the applicant.

It is the Examiners position that all the elements of Applicant's invention with respect to the specified claims are instantly disclosed by the teaching of the reference cited above.

8. Claims 21-24 remain rejected under 35 U.S.C. 103(a) as obvious over Lacroix et al (US 2002/0072864; filing date 08/31/1999). The reference teaches synthesizing

candidate structure(s) (see, e.g., claim 158). Although the reference does not teach specifically PCR method, such conventional method of protein synthesis would be an obvious choice to an artisan.

***Double Patenting***

8. Claims 12, 21-24, 33-35 remain provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 19-21 of copending Application No. 09/927790 in view of Wang et al (Pub. Med ID 8862547; Protein Engineering, 9(6),479-484, 1996) or Ulrich et al (Proteins: Structure, Function, and Genetics, 27,367-384, 1997).

Applicant requests that the rejection is reevaluated once the claims of both applications are in condition for allowance.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Borin whose telephone number is (571) 272-0713. The examiner can normally be reached on 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, Ph.D., can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Michael Borin, Ph.D.  
Primary Examiner  
Art Unit 1631



mlb  
11/03/2006



Substitute PTO/SB/08A (07-05)

Approved for use through 07/31/2006. OMB 0651-0031

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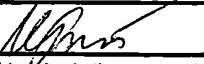
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| Substitute for form 1449/PTO<br>(Modified) |   |    |    | <b>Complete If Known</b> |                         |
|  |   |    |    | Application Number       | 09/782,004              |
|  |   |    |    | Filing Date              | February 12, 2001       |
|  |   |    |    | First Named Inventor     | Dahiyat et al.          |
|  |   |    |    | Art Unit                 | 1631                    |
|  |   |    |    | Examiner Name            | Borin, Michael          |
| Sheet                                      | 1 | of | 27 | Attorney Docket Number   | Docket 67299-6 463077-5 |

| U.S. PATENT DOCUMENTS |                       |   |                                |   |   |
|-----------------------|-----------------------|---|--------------------------------|---|---|
| Examiner Initials*    | Cite No. <sup>1</sup> | Document Number<br>Number-Kind Code <sup>2</sup> (if known) | Publication Date<br>MM-DD-YYYY | Name of Patentee or Applicant of Cited Document | Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear |
| MJ                    | A1                    | US-2002-0090648   | 07-11-2002                     | Dahiyat et al.                                  |   |
|                       | A2                    | US-2003-0049654   | 03-13-2003                     | Dahiyat et al.                                  |   |
|                       | A3                    | US-2004-0043429 A1  | 03-04-2004                     | Dahiyat et al.                                  |   |
|                       | A4                    | US-2004-0043430 A1  | 03-04-2004                     | Dahiyat et al.                                  |   |
|                       | A5 ↑                  | US-5436850  | 07-25-1995                     | Eisenberg et al.                                |   |
|                       | A6                    | US-6269312  | 07-31-2001                     | Mayo et al.                                     |   |

| FOREIGN PATENT DOCUMENTS |                       |   |                                |   |   |
|--------------------------|-----------------------|---|--------------------------------|---|---|
| Examiner Initials*       | Cite No. <sup>1</sup> | Foreign Patent Document<br>Country Code <sup>2</sup> Number <sup>3</sup> Kind Code <sup>5</sup><br>(if known) | Publication Date<br>MM-DD-YYYY | Name of Patentee or Applicant of Cited Document   | Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear |
|                          | B1 ↑                  | EP 0549107 A  | 06-30-1993                     | Syntex Inc.                                       |   |
|                          | B2 ↑                  | WO 00/40715 A   | 07-13-2000                     | Trustees of Boston University                     |   |
|                          | B3 ↑                  | WO 01/37147 A   | 05-25-2001                     | Algometrics NV                                    |   |
|                          | B4 ↑                  | WO 01/39098 A   | 05-31-2001                     | Yissum Research Development Company of the Hebrew |   |
|                          | B5 ↑                  | WO 01/61344 A   | 08-23-2001                     | California Institute of Technology                |   |
|                          | B6 ↑                  | WO 03/006154 A  | 01-23-2003                     | Xencor, Inc.                                      |   |
|                          | B7 ↑                  | WO 94/16090 A   | 07-21-2004                     | Molecular Tool, Inc.                              |   |
|                          | B8 ↑                  | WO 98/05765 A   | 02-12-1998                     | Novo Nordisk A/S                                  |   |
|                          | B9 ↑                  | WO 98/32845 A   | 07-30-1998                     | Bionvent International AB                         |   |

| NON PATENT LITERATURE DOCUMENTS |                       |   |  |  |                |
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| Examiner Initials*              | Cite No. <sup>1</sup> | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published. |  |  | T <sup>6</sup> |
|                                 | C1 ↑                  | Cojoc et al. "Seamless gene engineering using RNA- and DNA- overhang cloning" <i>Nature Biotechnology</i> , vol. 18, (2000) pps. 1087-0156  |  |  |                |
|                                 | C2 ↑                  | Gal J. et al. "Directional Cloning of Native PCR Products with Perfomed Sticky Ends" <i>Mol. Gen. Genet.</i> Vol. 260, no. 6, (1999), pps. 569-573  |  |  |                |
|                                 | C3                    | Koehl P. et al., "De novo protein design I. in search of stability and specificity" <i>J.Mol.Biol.</i> , vol. 293, no. 5, (1999) pps. 1161-1181   |  |  |                |
| MJ                              | C4 ↑                  | Wernisch L. et al. "Automatic protein design with all atom force-fields by exact and heuristic optimization" <i>J. Mol. Biol.</i> Vol. 301, no. 3, (2000), pps. 713-736   |  |  |                |

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|                    |   |                 |          |
|--------------------|---|-----------------|----------|
| Examiner Signature |  | Date Considered | 11/03/06 |
|--------------------|---|-----------------|----------|

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. <sup>1</sup>Applicant's unique citation designation number (optional). <sup>2</sup> See Kinds Codes of USPTO Patent Documents at [www.uspto.gov](http://www.uspto.gov) or MPEP 901.04. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup> Applicant is to place a check mark here if English Language Translation is attached.

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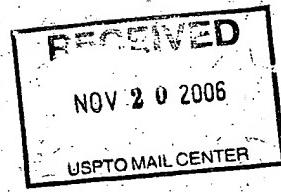
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